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## Self-reported Symptoms and Medical Conditions among 11,868 Gulf War-era Veterans

### The Seabee Health Study

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US Navy Seabees have been among the most symptomatic Gulf War veterans. Beginning in May 1997, the authors mailed Gulf War-era Seabees a health survey in serial mailings. As of July 1, 1999, 68.6% of 17,559 Seabees contacted had returned the questionnaire. Compared with other Seabees, Gulf War Seabees reported poorer general health, a higher prevalence of all 33 medical problems assessed, more cognition difficulties, and a higher prevalence of four physician-diagnosed multisymptom conditions: chronic fatigue syndrome, posttraumatic stress disorder, multiple chemical sensitivity, and irritable bowel syndrome. Because the four multisymptom conditions were highly associated with one another, the authors aggregated them into a working case definition of Gulf War illness. Among the 3,831 (22% cases) Gulf War Seabee participants, multivariable modeling revealed that female, Reserve, and enlisted personnel and participants belonging to either of two particular Seabee units were most likely to meet the case definition. Twelve of 34 self-reported Gulf War exposures were mildly associated with meeting the definition of Gulf War illness, with exposure to fumes from munitions having the highest odds ratio (odds ratio = 1.9, 95% confidence interval: 1.5, 2.4). While these data do not implicate a specific etiologic exposure, they demonstrate a strong association and a high prevalence of self-reported multisymptom conditions in a large group of symptomatic Gulf War veterans. *Am J Epidemiol* 2002;155:1033–44.

cross-sectional studies; health surveys; military medicine; military personnel; Persian Gulf syndrome; public health; veterans

Soon after the 1991 Persian Gulf War ended, veterans attributed illnesses they were experiencing to war exposures. Some of the earliest such reports came from members of US Naval Mobile Construction Battalions (NMCBs), or Seabees—particularly those attached to one Reserve battalion from the southeastern United States (1–3). In 1994, we conducted a cross-sectional survey of 1,497 Seabees who had remained on active duty after the war (4). We found that in comparison with their nondeployed peers, Gulf War Seabees reported a higher prevalence of 35 out of 41 symptoms, scored higher on psychological symptom scales, and were more likely to screen positive for posttraumatic stress disorder. However, despite numerous comparisons of these morbidity outcomes with 30 self-reported exposures, we

could not implicate a unique exposure or a group of exposures that might explain these Seabees' postwar symptoms. Additionally, in an attempt to identify a reputed Gulf War syndrome (5), we examined these symptom data using factor analysis techniques (6). Factor analysis yielded similar statistical aggregations of symptoms among both the Gulf War veterans and the nondeployed Gulf War-era Seabees. Since our 1994 study (4) involved only active-duty Seabees who had remained in service for 3 years after the war, we sought to study all Gulf War-era Seabees, including active-duty, Reserve, and separated personnel, to further explore the increased symptom reporting. This report summarizes the findings of this larger investigation.

### MATERIALS AND METHODS

#### Study population

For the purpose of this study, all regular and Reserve Navy personnel who had served on active duty in Seabee commands for at least 30 consecutive days between August 1, 1990, and July 31, 1991 (the Gulf War period) were eligible to participate, regardless of whether they were still in military service at the time of the study. The Seabee population was selected for several reasons. Members of a Reserve Seabee command issued some of the earliest and most persistent reports of postwar illnesses (1, 2, 7). The

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Abbreviation: NMCB, Naval Mobile Construction Battalion.

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work of the Seabees, which includes the building and maintenance of Navy and Marine Corps bases, ports, and field deployment facilities, both in the United States and around the world, subjects them to many unique environmental and occupational exposures, more so than most other military occupational groups. Between 1990 and 1991, a large component of the Seabee force remained stationed in the United States, while two other components were on foreign military deployment, either in support of the Gulf War or in one or more other foreign locations. This permitted us to examine the effects of deployment in the Persian Gulf theater of operations.

The study was approved by the institutional review board of the Naval Health Research Center (San Diego, California) and endorsed by the Institute of Medicine (Washington, DC) (1). It was conducted in compliance with all applicable federal regulations governing the protection of human subjects in research.

### Data collection

Postal addresses were obtained from the Defense Manpower Data Center (Seaside, California), from the Department of Veterans Affairs, and from commercial address-locator services. Seabees determined to be deceased by the Department of Veterans Affairs (before 1997) or by a survivor's response were removed from the mailing lists. The occupations of survey respondents and unit identification codes for the Gulf War time period were obtained from the Career History Archival Medical and Personnel System at the Naval Health Research Center (8). Geographic information systems data regarding possible exposure to smoke from oil-well fires and subclinical exposure to nerve agents were obtained as previously described (9, 10).

### Postal survey

We used an eight-page, 30-minute, optical-scan-formatted survey instrument derived from our previous Seabee survey (4) and a large Department of Veterans Affairs survey of Gulf War veterans (11). The questionnaire collected responses regarding family medical history, personal medical history, current symptoms, current health status, health-compromising behaviors, participation in either of the two federally sponsored Gulf War veteran registries (12), and environmental exposures. Because certain medications, particularly pyridostigmine bromide (13), have been theorized to be possible causes of Gulf War-related morbidity, photographs of pyridostigmine bromide, doxycycline, and ciprofloxacin tablets were included in the questionnaire as memory aids. The Cognitive Failures Questionnaire (14, 15) was included in the survey to assess the frequency of minor mental miscues that might explain the increased risk of accidents among some Gulf War Seabees (16). Prior to mailing, the survey was pilot-tested in a small group of Navy personnel; it was also critiqued by the Office of Management and Budget (Washington, DC) and by Department of Defense survey experts.

### Mailing procedures

Considerable effort was made to obtain a completed questionnaire from each of the 18,945 potential study subjects. After a postcard was sent to each subject in May 1997 to confirm his or her address, a series of questionnaires were mailed at approximately 5-month intervals. Each questionnaire was followed approximately 2 weeks later by a reminder postcard.

Cover letters from a senior commander of the NMCBs and the Naval Health Research Center were enclosed with outgoing questionnaires to explain the study and the importance of participation. Care was taken to emphasize the voluntary nature of participation, the confidentiality of participant data, and the fact that nonparticipants would not be penalized in any way. A nonmonetary incentive—a photograph of the Seabee Memorial in Arlington, Virginia, a mechanical pencil, or a prepaid telephone calling card—was included in all questionnaire mailings.

Returned questionnaires were manually checked for errors and completeness before error-detecting optical scanning was performed.

### Nonrespondent telephone survey

In an effort to assess the representativeness of respondents for the target Seabee population, we randomly selected 500 nonrespondents whose surveys had not been returned by the US Postal Service. Employees of the Social Science Research Laboratory at San Diego State University (San Diego, California) then endeavored to find and win the participation of these individuals in a nonrespondent telephone survey. The nonrespondent questionnaire was designed to take approximately 7 minutes. It consisted of selected items from the original questionnaire, including questions on Gulf War status, health history, symptoms, exposures, and current health habits.

### Statistical analyses

Univariate comparisons of demographic and symptom variables by study group were made using the Wilcoxon rank sum or Pearson chi-squared test of association. Where cell counts were sparse, Fisher's exact test was used to determine whether a univariate association existed. Age as of July 31, 1990, was established. Marital status at the time of the Gulf War was determined from Defense Manpower Data Center records. Gulf War service was determined by the subject's response to a question regarding military service in the Persian Gulf during the Gulf War. Odds ratios and 95 percent confidence intervals were computed using either the Cornfield method or the exact method (17). Multivariable logistic regression modeling was performed using both a saturated model and a backward manual elimination procedure.

## RESULTS

### Participation

Using questionnaire responses and deployment data from the Defense Manpower Data Center for the Gulf War period,

we stratified Seabees into three groups: those deployed to the Gulf War theater (18) for 1 or more days during the Gulf War period (Gulf War Seabees); those deployed outside of the United States but not to the Gulf War theater (Seabees deployed elsewhere); and nondeployed Seabees.

Among the 18,945 subjects the Defense Manpower Data Center identified as assigned to Seabee units between August 1, 1990, and July 31, 1991, 17,559 received a study questionnaire in the course of multiple mailings conducted between May 1997 and May 1999. By July 1, 1999, 12,049 (68.6 percent) of these potential subjects had returned a questionnaire. Of the 12,049 questionnaires returned, 181 were blank. Thus, we received questionnaire data from 11,868 Seabees: 3,831 Gulf War Seabees, 4,933 Seabees deployed elsewhere, and 3,104 nondeployed Seabees. Approximately 56 percent, 30 percent, and 15 percent of 11,868 Seabee respondents returned completed questionnaires during mailings 1, 2, and 3, respectively. Participants

were more likely to be reservists, to be married, to be Caucasian, and to be among the group of Seabees deployed elsewhere than in the Persian Gulf (table 1).

#### Survey findings by Seabee group

In comparisons of the three Seabee groups (tables 1 and 2), Gulf War Seabees were more often reservists, male, and unmarried, were slightly younger, had more evidence of cognitive failure (a higher mean score on the Cognitive Failures Questionnaire), and reported more days lost due to illness in the previous 12 months than the other two groups. Change in body mass index between 1990 and 1998 did not differ between the three Seabee groups.

Compared with the other two groups (table 3), Gulf War Seabees were more likely to be smokers or to have been smokers in the past. They were more likely to report that newly diagnosed digestive diseases or depression had caused

**TABLE 1. Demographic characteristics (%) of participants as compared with potential study subjects, Seabee Health Study, 1997–1999**

Characteristic	Target population (n = 18,945)	Respondents (n = 11,868)	Gulf War Seabees (n = 3,831)	Seabees deployed elsewhere (n = 4,933)	Nondeployed Seabees (n = 3,104)
<b>Deployment</b>					
Gulf War Seabees	32.8	32.3	100.0		
Seabees deployed elsewhere	14.7	41.6		100.0	
Nondeployed Seabees	52.0	26.2			100.0
Unknown	0.5	0.0			
<b>Service type</b>					
Regular active duty	88.4	86.5	77.6	92.5	88.1
Reserves	11.6	13.5	22.4	7.5	11.9
<b>Gender</b>					
Male	95.4	95.5	98.9	94.7	92.8
Female	4.7	4.5	1.1	5.3	7.3
<b>Marital status</b>					
Married	58.4	62.4	55.5	62.9	70.0
Unmarried	41.2	37.6	44.5	37.1	30.0
Missing data	0.4	0.0	0.0	0.0	0.0
<b>Race</b>					
Caucasian	85.0	87.9	87.5	87.5	89.2
Black	10.0	7.1	7.9	7.4	5.9
Other	5.0	5.0	4.7	5.2	5.0
<b>Occupation</b>					
Enlisted personnel	(n = 16,980)	(n = 10,244)	(n = 3,632)	(n = 4,329)	(n = 2,283)
Builder	24.6	24.3	23.3	25.4	23.9
Equipment operator	17.8	18.5	19.4	17.4	19.2
Construction mechanic	13.6	14.2	14.7	13.4	15.0
Construction electrician	11.0	11.2	10.2	12.2	11.0
Utility person	9.6	9.8	8.3	10.8	10.0
Steelworker	7.0	7.0	7.8	6.9	6.0
Engineering aide	2.7	3.0	2.6	3.4	2.9
Other enlisted person	12.9	11.9	13.7	10.5	11.9
Missing data	0.8	0.1	0.0	0.0	0.1
Officers	(n = 1,965)	(n = 1,624)	(n = 199)	(n = 604)	(n = 821)
Civil engineering corps	86.2	85.8	73.4	89.7	86.0
Other officer	13.8	14.2	26.6	10.3	14.0
Missing data	0.1	0.0	0.0	0.0	0.0

**TABLE 2. Selected characteristics of US Navy Seabees by deployment group, Seabee Health Study, 1997–1999**

Characteristic	Gulf War Seabees (n = 3,831)	Seabees deployed elsewhere (n = 4,933)	Nondeployed Seabees (n = 3,104)
Mean age (years) in 1990	29.0	30.1	33.3
Mean change in body mass index* from 1990 to 1998†	1.5	1.5	1.6
Mean score on the Cognitive Failures Questionnaire	42.4	32.6	32.0
Mean no. of days unable to work due to illness in the past 12 months	8.7	5.1	8.0

\* Weight (kg)/height (m)<sup>2</sup>.

† The year 1998 was used as an average of 1997–1999.

them to lose 1 or more weeks of school or work and were more likely to report having had one or more hospitalizations since August 1990. Gulf War Seabees were also more likely to report being in fair or poor health at the time of survey completion and to report having physician-diagnosed ill-

nesses (table 4). With the exception of leishmaniasis, the physician-diagnosed illnesses most strongly associated with Gulf War service were multisymptom conditions: chronic fatigue syndrome, posttraumatic stress disorder, multiple chemical sensitivity, and irritable bowel disease. Similarly, when respondents were asked to consider medical problems they had experienced during the previous 12 months, Gulf War Seabees were more likely to self-report all 33 problems queried about (table 5).

When responses to the 33 questions on medical problems were counted (table 5), Gulf War Seabees who reported having at least one of the four physician-diagnosed multisymptom conditions (table 4) were very symptomatic in comparison with their peers. Gulf War Seabees who reported having chronic fatigue syndrome, posttraumatic stress disorder, multiple chemical sensitivity, and irritable bowel disease averaged 16.3, 17.8, 17.0, and 13.6 medical problems, respectively, while other Gulf War Seabees reported a mean of only 6.0 problems.

Among Gulf War Seabees, there was a high correlation between the four multisymptom conditions, having a score of  $\geq 42$  on the Cognitive Failures Questionnaire, and self-reporting of 12 or more medical problems. The cutpoint of  $\geq 12$  was chosen because, for each of the four multisymptom conditions, this cutpoint captured more than 50 percent of respondents who self-reported that condition. The odds

**TABLE 3. Prevalences of and unadjusted odds ratios for self-reported health behaviors and other health-related factors by deployment group, Seabee Health Study, 1997–1999**

Health factor	Affirmative response (%)			Gulf War Seabees versus Seabees deployed elsewhere		Gulf War Seabees versus nondeployed Seabees	
	Gulf War Seabees (n = 3,831)	Seabees deployed elsewhere (n = 4,933)	Nondeployed Seabees (n = 3,104)	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval
<b>Health behavior</b>							
Ever smoking	55.04	53.25	46.29	1.08	0.99, 1.17	3.09	2.79, 3.42
Current smoking	42.71	37.38	30.55	1.20	1.09, 1.31	2.68	2.37, 3.04
Alcohol drinking from August 1989 to July 1990	79.49	81.61	77.21	0.87	0.78, 0.97	1.17	1.04, 1.31
Alcohol drinking in February 1991	35.01	77.99	71.57	0.16	0.14, 0.17	0.22	0.20, 0.25
Current alcohol drinking	66.19	68.83	64.62	0.88	0.81, 0.97	1.08	0.98, 1.20
<b>New illnesses diagnosed since August 1990</b>							
Cancer	0.55	0.61	1.00	0.90	0.51, 1.58	0.55	0.31, 0.95
Hepatitis	0.50	0.29	0.36	1.75	0.88, 3.50	1.40	0.67, 2.95
Digestive diseases	2.16	0.96	1.04	2.27	1.58, 3.26	2.10	1.39, 3.17
Lung diseases	0.82	0.57	0.49	1.43	0.86, 2.39	1.68	0.91, 3.12
Depression	2.96	1.29	2.18	2.33	1.70, 3.18	1.37	1.00, 1.85
<b>No. of hospitalizations since August 1990*</b>							
0	60.17	63.67	63.56	0.86	0.79, 0.94	0.87	0.79, 0.95
$\geq 1$	39.83	36.33	36.44	1.16	1.06, 1.27	1.15	1.05, 1.27
<b>Present health*</b>							
Very good/excellent	39.78	59.98	58.73	0.44	0.40, 0.48	0.46	0.42, 0.51
Good	37.61	29.01	27.87	1.48	1.35, 1.61	1.56	1.41, 1.73
Fair/poor	20.44	8.92	11.57	2.62	2.31, 2.97	1.96	1.72, 2.25

\* Percentages do not total 100% because some veterans did not respond.

TABLE 4. Self-reported health outcomes by deployment group, Seabee Health Study, 1997–1999\*

Self-reported physician-diagnosed illness	Affirmative response (%)			Gulf War Seabees versus Seabees deployed elsewhere		Gulf War Seabees versus nondeployed Seabees	
	Gulf War Seabees (n = 3,831)	Seabees deployed elsewhere (n = 4,933)	Nondeployed Seabees (n = 3,104)	Odds ratio†	95% confidence interval	Odds ratio†	95% confidence interval
Leishmaniasis	0.50	0.04	0.00	6.76	1.52, 30.13		
Chronic fatigue syndrome	5.17	0.79	0.68	5.76	4.03, 8.24	7.60	4.76, 12.13
Posttraumatic stress disorder	3.08	0.61	0.71	4.27	2.79, 6.52	4.23	2.59, 6.92
Multiple chemical sensitivity	1.62	0.32	0.39	4.08	2.29, 7.24	4.47	2.30, 8.69
Irritable bowel syndrome	2.48	0.67	0.81	3.54	2.32, 5.39	3.57	2.22, 5.73
Cirrhosis	0.23	0.08	0.23	3.60	0.94, 13.82	1.30	0.45, 3.79
Skin rash	20.28	7.64	5.64	3.07	2.67, 3.52	4.22	3.51, 5.07
Impotence	2.27	0.93	0.97	2.23	1.51, 3.27	3.06	1.95, 4.83
Depression	7.73	3.67	4.61	2.10	1.72, 2.58	1.77	1.41, 2.27
Peptic ulcer disease	1.54	0.71	0.45	2.14	1.38, 3.34	3.11	1.67, 5.78
Migraines	6.60	3.14	2.58	2.24	1.80, 2.78	2.71	2.04, 3.60
Tinnitus	6.53	3.79	4.16	1.75	1.43, 2.15	1.86	1.47, 2.36
Lumbago	4.05	2.45	1.84	1.67	1.29, 2.15	2.49	1.78, 3.47
Bronchitis	7.36	4.54	4.38	1.55	1.28, 1.88	1.49	1.18, 1.87
Thyroid condition	1.15	0.69	0.97	1.87	1.16, 3.03	1.49	0.89, 2.50
Hypertension	8.09	5.41	5.38	1.63	1.36, 1.95	1.82	1.48, 2.26
Prostatitis	2.38	1.58	1.90	1.38	0.99, 1.91	1.54	1.07, 2.21
Mononucleosis	0.55	0.36	0.23	1.66	0.85, 3.21	1.99	1.80, 4.96
Urinary tract infection	4.62	3.14	2.32	1.55	1.23, 1.96	2.50	1.83, 3.44
Kidney disease	0.34	0.24	0.26	1.18	0.52, 2.69	1.57	0.61, 4.05
Asthma	2.38	1.72	1.45	1.36	0.99, 1.87	1.82	1.23, 2.69
Arthritis	5.87	4.42	4.38	1.44	1.17, 1.76	1.63	1.29, 2.08
Diabetes mellitus	1.04	0.91	1.61	1.06	0.67, 1.68	0.77	0.49, 1.23
Kidney stones	2.57	2.27	2.19	0.86	0.65, 1.14	1.08	0.77, 1.51

\* Only conditions with an onset after August 1991 were counted.

† Odds ratios were derived by logistic regression analysis and were adjusted for age, gender, active-duty/Reserve status, race/ethnicity, current smoking, and current alcohol drinking.

ratios for a Gulf War Seabee with one multisymptom condition having another multisymptom condition ranged from 5.3 to 30.4 (table 6); this suggests that being diagnosed with one of these multisymptom conditions or reporting 12 or more of the 33 medical problems distinguished ill veterans from non-ill veterans.

### Self-reported Gulf War exposures

Gulf War Seabee respondents were asked questions regarding their experience with 34 possible exposures during their service in the Persian Gulf. The percentage responding affirmatively to these questions ranged from 91 percent for receipt of typhoid vaccine to 4 percent for exposure to pesticides (data not shown).

### Risk factors for Gulf War illness

For the purpose of risk factor modeling and for reasons discussed below, we defined a case of Gulf War illness as having any one of five conditions: a self-reported physician diagnosis of chronic fatigue syndrome, posttraumatic stress disorder, multiple chemical sensitivity, or inflammatory bowel disease (table 4) or self-reporting of 12 or more med-

ical problems (table 5). Among Gulf War Seabees, 845 (22.1 percent) of the 3,831 respondents met the case definition. Among these 845 cases of Gulf War illness, 126 met the case definition solely on the basis of self-reporting of 12 or more medical problems. Among Gulf War Seabees, the odds of reporting participation in either of the federally sponsored Gulf War veteran registries (12) were higher among those who met the case definition than among those who did not (odds ratio = 5.6, 95 percent confidence interval: 4.7, 6.8).

Considering only Gulf War Seabees, we next evaluated demographic risk factors (tables 1 and 2), current smoking or alcohol drinking (table 3), self-reported Persian Gulf exposures (table 7), period of service in the Gulf War theater, and exposure to oil-well-fire smoke (10) for associations with the case definition of Gulf War illness. No Seabees had been located under the atmospheric plume subsequent to the March 1991 destruction of munitions at the Khamisiyah site (9). Demographic covariates included service type, gender, age, education, marital status, race/ethnicity, Seabee unit during deployment, and occupation. To simplify modeling and yet permit examination of effect, we stratified age into quartiles. Time period of service in the Gulf War theater was derived from responses to the questionnaire.

**TABLE 5. Self-reported persistent or recurring medical problems experienced during the 12 months prior to taking the survey, Seabee Health Study, 1997–1999\***

Self-reported medical problem	Affirmative response (%)			Gulf War Seabees versus Seabees deployed elsewhere		Gulf War Seabees versus nondeployed Seabees	
	Gulf War Seabees (n = 3,831)	Seabees deployed elsewhere (n = 4,933)	Nondeployed Seabees (n = 3,104)	Odds ratio†	95% confidence interval	Odds ratio†	95% confidence interval
Multiple chemical sensitivity	4.25	0.67	0.71	5.49	3.72, 8.12	5.95	3.71, 9.55
Nightmares/flashbacks	11.77	2.59	2.29	4.58	3.72, 5.64	4.58	3.50, 6.00
Rash or skin ulcer	22.37	6.12	5.06	4.13	3.58, 4.78	4.85	4.02, 5.85
General muscle weakness	16.29	4.62	4.19	3.69	3.13, 4.35	4.11	3.34, 5.06
Unusual irritability	27.15	8.55	7.06	3.73	3.28, 4.24	4.25	3.60, 5.02
Unusual muscle pains	22.58	6.85	5.67	3.58	3.12, 4.12	4.41	3.68, 5.28
Chills	8.98	2.45	2.55	3.51	2.81, 4.37	3.14	2.41, 4.10
Short-term memory problems	39.49	14.33	12.85	3.59	3.23, 4.00	3.93	3.45, 4.49
Unusual fatigue	38.95	14.13	13.43	3.62	3.25, 4.03	3.65	3.20, 4.16
Frequent rage	17.83	5.66	4.99	3.29	2.83, 3.83	3.31	2.73, 4.02
Night sweats	17.12	5.45	4.61	3.23	2.76, 3.77	3.67	3.00, 4.47
Sudden hair loss	6.37	1.86	1.80	3.33	2.58, 4.30	3.05	2.23, 4.16
Shortness of breath	16.08	5.29	4.54	3.14	2.68, 3.68	3.62	3.01, 4.51
Joint stiffness	30.10	11.23	9.79	3.18	2.83, 3.58	3.85	3.32, 4.46
Sleepiness	22.61	8.03	6.83	3.16	2.77, 3.62	3.38	2.85, 4.01
Diarrhea	24.04	8.86	6.77	2.98	2.62, 3.39	3.75	3.17, 4.44
Bleeding gums	10.42	3.49	2.42	2.90	2.40, 3.51	3.91	3.00, 5.10
Continual cough	9.50	3.22	3.16	3.03	2.48, 3.71	2.70	2.11, 3.44
Trouble sleeping	38.58	16.70	15.46	3.02	2.72, 3.35	3.08	2.71, 3.50
Depression	17.65	6.55	6.02	2.83	2.44, 3.28	3.07	2.55, 3.69
Joint pain	37.85	16.81	13.60	2.83	2.56, 3.14	3.65	3.20, 4.16
Chronic worry/anxiety	17.93	6.83	6.31	2.89	2.50, 3.34	2.79	2.33, 3.34
Appetite loss	9.37	3.43	3.03	2.69	2.21, 3.28	2.54	1.98, 3.26
Chest pain	16.00	6.12	5.09	2.72	2.34, 3.17	3.06	2.52, 3.71
Stomach pain/ulcer	13.44	5.05	4.35	2.75	2.33, 3.24	3.08	2.49, 3.80
Severe headache	26.89	11.31	9.83	2.80	2.48, 3.15	3.03	2.60, 3.52
Constipation	6.89	2.55	2.29	2.74	2.18, 3.45	2.78	2.09, 3.71
Sudden weight loss	6.94	2.70	2.03	2.60	2.08, 3.25	2.99	2.22, 4.03
Sore throat	16.00	6.73	5.67	2.52	2.17, 2.92	2.98	2.47, 3.61
Suicidal thoughts	6.42	2.59	2.67	2.40	1.90, 3.01	2.16	1.64, 2.84
Sudden weight gain	12.03	5.03	4.38	2.50	2.11, 2.96	3.11	2.50, 3.86
Joint swelling/redness	11.38	5.21	3.67	2.28	1.93, 2.70	3.39	2.71, 4.26
Marital stress	19.45	10.12	7.70	1.99	1.75, 2.26	2.61	2.21, 3.08

\* Only conditions with an onset after August 1991 were counted.

† Odds ratios were derived by logistic regression analysis and were adjusted for age, gender, active-duty/Reserve status, race/ethnicity, current smoking, and current alcohol drinking.

**TABLE 6. Unadjusted odds ratios for self-reporting of one physician-diagnosed multisymptom condition given the self-report of another physician-diagnosed multisymptom condition among 3,831 Gulf War Seabees, Seabee Health Study, 1997–1999**

	Chronic fatigue syndrome	Posttraumatic stress disorder		Multiple chemical sensitivity		Irritable bowel syndrome		≥12 medical problems*		CFQ† score ≥42	
		Odds ratio	95% CI†	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI
Chronic fatigue syndrome	N/A†	30.4	20.3, 45.3	24.9	14.7, 41.9	10.4	6.6, 16.3	12.1	8.8, 16.6	5.5	3.7, 8.2
Posttraumatic stress disorder				15.0	8.4, 26.9	7.8	4.5, 13.7	19.4	12.3, 30.5	9.1	5.0, 16.6
Multiple chemical sensitivity						14.7	7.9, 27.4	11.2	6.4, 19.5	11.5	4.6, 28.9
Irritable bowel syndrome								5.3	3.5, 8.0	3.3	2.1, 5.4
≥12 medical problems*										12.7	9.9, 16.4
CFQ score ≥42										N/A	

\* Participant self-reported having 12 or more medical problems out of a possible 33 problems during the 12 months before taking the survey.

† CFQ, Cognitive Failures Questionnaire; CI, confidence interval; N/A, not applicable.

Consistent with other reports (19–22), univariate modeling revealed that many self-reported Gulf War exposures were mildly associated with illness (table 7). Among the 34 exposure questions, only the drinking of diet soda during the Gulf War was not so associated. Other risk factors with significant univariate associations with Gulf War illness included service type, exposure to oil-well-fire smoke (10), gender, occupation, and assignment to certain NMCBs (table 7). In logistic regression analysis, the final backward-elimination multivariable model revealed that females, Reserve personnel, persons not exposed to smoke from oil-well fires, enlisted persons without traditional Seabee occupations, and Gulf War Seabees assigned to NMCB 40 or NMCB 133 were more likely to meet the definition of Gulf War illness (table 7). Twelve Gulf War-related exposures were weakly associated with the case definition. As is evidenced by the saturated multivariable model, several other Gulf War-related exposure covariates approached statistical significance (table 7).

### Survey reliability

Because of postal time lags and labeling errors, 824 respondents received and completed two questionnaires. These 824 respondents were older than the respondents who completed only one questionnaire, were less likely to have been deployed abroad, and had a higher educational level. In an effort to assess the reliability of survey responses, we selected a stratified random sample (by age, education, and deployment abroad—30 cells) to identify a subset of 519 double respondents that was demographically representative of the total respondent population.

On average, the 519 respondents completed the surveys approximately 6 months apart. Kappa statistics were high for Gulf War deployment ( $\kappa = 0.92$ ), exposures in the Gulf War (mean  $\kappa = 0.74$ ), demographic data (mean  $\kappa = 0.69$ ), deployment abroad ( $\kappa = 0.69$ ), having certain diseases during one's lifetime (mean  $\kappa = 0.67$ ), family history of disease (mean  $\kappa = 0.67$ ), behavioral risk factors (mean  $\kappa = 0.65$ ), and physician-diagnosed medical conditions (mean  $\kappa = 0.60$ ). Kappa statistics were lower for more time-sensitive questions, such as questions on present medical conditions (mean  $\kappa = 0.51$ ), self-reported general health status ( $\kappa = 0.47$ ), participation in a federal Gulf War veteran registry ( $\kappa = 0.43$ ), and cognitive failure (mean  $\kappa = 0.31$ ) (data not shown).

### Nonrespondent telephone survey

After extensive searching, 194 postal-survey nonrespondents completed the telephone interview. One subject subsequently submitted the postal survey and was reclassified as a respondent. Forty-seven nonrespondents (24 percent) told the interviewer that they had never received the questionnaire in the mail. Seven (4 percent) were uncertain about whether they had received the postal survey. Among the 139 subjects who remembered receiving the questionnaire, reasons for their lack of response were varied: 91 (66 percent) reported not responding for personal or subjective reasons,

26 (19 percent) considered themselves ineligible, 21 (15 percent) claimed to have completed the questionnaire and mailed it, and one declined to answer the question.

Demographically, the 193 nonrespondents were slightly younger than respondents and were less likely than respondents to be currently serving in the military, but otherwise they were not different with respect to gender, race/ethnicity, marital status, employment, or education. Nonrespondents were more likely to have registered with the Department of Defense Gulf War Registry but were not at increased odds of participating in the similar Department of Veterans Affairs Gulf War Registry. Nonrespondents drank less alcohol and smoked more than respondents. They reported more arthritis and more depression, but they were similar to respondents with respect to physician-diagnosed conditions, other illnesses, and self-reported number of hospitalizations since 1990 (data not shown). With their many similarities, we feel that our respondents were good representatives of the cohort of 18,945 Gulf War-era Seabees.

### DISCUSSION

Gulf War veterans often report medical symptoms. This is particularly true for a group of Reserve Seabees who were deployed to the Gulf War theater with NMCB 24. Soon after the war ended, their complaints of unexplained symptoms were evaluated by a Navy outbreak investigation team (1), news reporters (23–26), a Congressional survey (27), and a team of investigators from the University of Texas Southwestern Medical Center (3). We sought to better understand the increased Seabee symptom reporting to determine whether it was more prevalent in NMCB 24 compared with other Seabee units and to examine associations between self-reported symptoms and Gulf War exposures for possible etiologic insights.

Our first task was to compare the self-reported morbidity of Gulf War Seabees with that of other Seabees from the same era. Although there were some statistical differences, the three Seabee groups were very similar in terms of their demographic composition (table 1). However, Gulf War Seabees reported more digestive diseases, depression, hospitalizations, and lost workdays and poorer present health than the other two groups (tables 2 and 3). Gulf War Seabees also reported more physician-diagnosed chronic fatigue syndrome, posttraumatic stress disorder, multiple chemical sensitivity, and irritable bowel syndrome, as well as a number of other conditions (table 4). Consistent with our previous Seabee study (4) and with symptom studies from other research groups (11, 19–21, 28–30), Gulf War Seabees self-reported more symptoms than the two other Seabee groups.

Considering the increased morbidity findings, we next sought to separate the most symptomatic Gulf War Seabees to examine them more closely and to consider their specific Gulf War exposures for possible etiologies. Four self-reported physician diagnoses with strong associations with Gulf War service (table 4) could be classified as multisymptom conditions: chronic fatigue syndrome, posttraumatic stress disorder, multiple chemical sensitivity, and irritable bowel syndrome. We found very strong associations between

TABLE 7. Risk factors for meeting the case definition of Gulf War illness among 3,831 Gulf War Seabees, Seabee Health Study, 1997-1999

Risk factor	Univariate modeling		Saturated multivariable model*		Backward-elimination multivariable model†	
	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval
Age (years)‡						
22-26	0.98	0.82, 1.16	1.01	0.77, 1.33		
27-34	0.72	0.59, 0.88	0.89	0.65, 1.22		
35-59	1.30	1.10, 1.56	1.02	0.74, 1.43		
Gender (female vs. male)	1.99	1.03, 3.84	3.64	1.50, 8.83	3.23	1.39, 7.53
Marital status	1.15	0.98, 1.35	1.21	0.97, 1.50		
Service type (Reserves vs. regular active duty)	1.74	1.46, 2.08	1.81	1.18, 2.78	1.70	1.18, 2.43
Deployment period						
August 1990-October 1990	0.74	0.63, 0.87	1.03	0.74, 1.44		
November 1990-January 1991	1.30	1.07, 1.57	1.12	0.81, 1.54		
Exposure to smoke from oil-well fires (yes vs. no)§	1.54	1.31, 1.80	0.43	0.25, 0.75	0.44	0.26, 0.73
Occupation						
Builder	0.93	0.71, 1.22	0.95	0.67, 1.34	1.05	0.76, 1.45
Equipment operator	1.02	0.77, 1.35	0.93	0.65, 1.33	1.01	0.72, 1.41
Construction mechanic	1.05	0.79, 1.42	0.95	0.66, 1.38	1.09	0.77, 1.54
Construction electrician	0.84	0.60, 1.18	0.84	0.55, 1.27	0.89	0.60, 1.32
Utility person	1.08	0.77, 1.53	0.93	0.60, 1.43	1.06	0.70, 1.59
Steelworker	0.68	0.46, 0.99	0.66	0.41, 1.04	0.74	0.47, 1.15
Engineering aide	1.15	0.69, 1.93	1.21	0.63, 2.34	1.36	0.73, 2.53
Civil engineering officer	0.14	0.06, 0.33	0.14	0.05, 0.37	0.15	0.06, 0.39
Other officer	0.46	0.19, 1.11	0.33	0.10, 1.11	0.50	0.17, 1.45
Military unit#						
NMCB** 24	1.64	1.27, 2.11	1.41	0.77, 2.58	1.47	0.84, 2.57
NMCB 4	0.57	0.41, 0.80	1.58	0.97, 2.58	1.32	0.86, 2.01
NMCB 5	0.98	0.74, 1.30	1.51	0.82, 2.81	1.38	0.79, 2.39
NMCB 7	0.54	0.39, 0.76	1.15	0.68, 1.95	1.09	0.70, 1.69
NMCB 40	1.20	0.92, 1.57	2.20	1.16, 4.15	2.15	1.22, 3.81
NMCB 133	0.80	0.58, 1.12	2.21	1.30, 3.78	1.81	1.15, 2.84
NMCB 74	1.11	0.84, 1.46	1.52	0.81, 2.86	1.39	0.80, 2.47

[illegible]

\* Data for 648 Seabees were incomplete and were not included in the saturated multivariate model.

\* \* Data for 648 Seabees were incomplete and were not included in the saturated multivariate model.

† Reference group: age 17–21 years.

§ As measured by geographic information systems mapping (10).

¶ Reference group: other enlisted personnel.

# Reference group: other Seabee units. Thirteen percent of the other Seabee units comprised Reserve personnel.

\* NMCB, Naval Mobile Construction Battalion.

these conditions among Gulf War Seabees (table 6). Since previous research has demonstrated much overlap between these diagnoses (31–33), since Gulf War veteran groups have reported high prevalences of these conditions (19, 21, 28, 29, 34–37), since using these diagnoses depends on clinician training (38), since there is a long history of multisymptom sequelae after wars (39, 40), and since numerous research teams have tried and failed to identify a specific Gulf War syndrome (6, 41–43), we aggregated the four diagnoses in a working case definition of Gulf War illness. Realizing that not all very symptomatic Gulf War Seabees seek medical evaluation and thus not all could have received the diagnosis of a multisymptom condition, we also classified Gulf War Seabees who self-reported 12 or more medical problems (table 5) as having evidence of Gulf War illness.

This definition of Gulf War illness was then used to evaluate possible risk factors for illness. Our finding of increased odds of Gulf War illness among female Reserve personnel is consistent with our previous work (12) and that of another research team (44). Our data suggest that once Reserve status was controlled for, personnel assigned to NMCB 24 were not more symptomatic than their peers from other Seabee units. Instead, Seabees who served with the regular active-duty units NMCB 40 and NMCB 133 had slightly increased odds of illness as compared with other Seabee units. Unfortunately, the reason for this increase in risk is unclear, as the two units were deployed to the Gulf War theater during different time periods and served in different locations. NMCB 40 served in Saudi Arabia at Al Jabail (Camp Rohrbach), Tanajim, and Al Qaraah from September 1990 through March 1991. NMCB 133 served in Iraq at Sikh, Sakho, and Sirsenk in April and May 2001.

Our findings of multiple weak associations between Gulf War exposures and Gulf War illness are consistent with our previous work (4) and that of some other research teams (19, 22, 28). However, we did not find independent associations between Gulf War illness and exposure to direct combat (45), exposure to dead bodies (45), receipt of botulism vaccine (46), receipt of anthrax vaccine (21), wearing a uniform that had been treated with insect repellent (44), or time period in the Gulf theater (29). Similarly, while we found a mild increase in the odds of Gulf War illness among participants who reported ingesting pyridostigmine bromide, the magnitude of this association was not as strong as that found by another research team (44).

More interesting among our observed statistical associations was the clear association between Gulf War illness and a high score on the Cognitive Failures Questionnaire. We believe we are the first to have used this instrument among Gulf War veterans. Gulf War Seabees have long complained of memory problems, and other research teams have found evidence of cognitive deficits (19, 28). However, our findings must be balanced by our discovery of the rather poor reliability of the questionnaire. While this may be partially explained by the average gap of 6 months between surveys, we believe that cognitive function is better evaluated through specialized neurocognitive testing.

This study had a number of limitations. With so many statistical comparisons, it is likely that at least some of our pos-

itive associations occurred by chance alone. All morbidity and exposure data were self-reported. Our work (4) and that of others (47) has demonstrated that recall bias is a very real problem among Gulf War Seabees. It is likely that some Gulf War Seabees were influenced by news stories (12), previous survey participation, or the mailings sent to more than 300,000 Gulf War veterans by the Defense Department's Office of the Special Assistant for Gulf War Illnesses. These factors may have caused veterans to report more symptoms and exposures than they otherwise might have reported. Some Gulf War Seabees may have associated study participation with possible financial compensation and inflated their survey responses. While these limitations are very real for studies of Gulf War veterans, the Department of Defense has reduced the future likelihood of such problems by more aggressive collection of health data prior to and after deployments, as well as collection of comprehensive data on exposures incurred during deployments. These new efforts comprise a shift in medical policy termed "Force Health Protection" by the Department of Defense (48).

The Force Health Protection strategy resulted partly from the advice of numerous expert review panels (49–51). The many new preventive initiatives are beyond the scope of this paper, but two such efforts deserve mention. The first is the eventual screening of all new military personnel for potential risk factors for postdeployment multisymptom morbidity (52). If such risk factors can be identified, such personnel might be given special training to prepare them for the stresses of deployment. There is considerable evidence that such a training strategy would be effective (53–55). The second important new development is implementation of the Millennium Cohort Study, a 21-year prospective study of 140,000 service personnel and the health effects of military service (56, 57). Closely following a cohort of this size using serial surveys will enable investigators to examine many hypotheses regarding possible military service-associated illnesses.

Our study had a number of strengths. To our knowledge, it represents the third-largest controlled survey of Gulf War veterans to date. Only the US Department of Veterans Affairs study (11) and the UK University of Manchester study (58) have been larger. We achieved excellent rates of participation. If one adds the 194 telephone interview respondents, 12,243 members (69.7 percent) of the located target population responded to the survey. Alternatively, if one extrapolates from the data acquired from the telephone interview and assumes that 24 percent ( $n = 1,322$ ) of the 5,510 potential subjects who failed to respond to the mailed survey never received a questionnaire, our original response estimate increases to 74.2 percent (12,049/16,237). This participation rate of approximately 70 percent is consistent with the highest responses to Gulf War veteran surveys. Our study was also unique in its use of visual aids to reduce recall bias concerning ingestion of doxycycline, ciprofloxacin, and pyridostigmine bromide. Finally, our study suggested that Gulf War Seabees report more cognitive problems than their non-Gulf Seabee peers.

We conclude that Gulf War Seabees report more postwar morbidity than their Gulf War-era peers. This morbidity is

often diagnosed as a multisymptom condition, and the four such diagnoses examined in this study were highly correlated. This morbidity may be associated with an increased risk of hospitalization, may involve problems with cognition, and may be associated with an increased risk of physician diagnosis of certain illnesses, such as depression and migraine headaches. When a working case definition of Gulf War illness was defined and Gulf War Seabees were studied separately, Seabees who were enlisted, Reserve, or female or who belonged to either of two particular Seabee units were more likely to meet the case definition. Twelve Gulf War exposures were mildly associated with illness, but the exposure associations appeared too weak and disparate to support a cohesive explanation of postwar morbidity. Instead, the aggregate stresses of war seem to be a more plausible etiology.

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13. SUPPLEMENTARY NOTES

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14. ABSTRACT (maximum 200 words)

Gulf War veterans have complained of postwar morbidity that they attribute to their military service. US Navy construction workers (Seabees) have been among the most symptomatic. Beginning in 1997, we sent Gulf War-era Seabees a postal survey to collect information regarding their past and present health. After serial mailings, 12,049 (68.5%) of 17,559 Seabees contacted returned the questionnaire. Compared with other Seabees, Gulf War Seabees self-reported poorer general health, more depression, a higher prevalence of all 33 symptom questions, and higher prevalences of physician-diagnosed four multi-symptom conditions: chronic fatigue syndrome, posttraumatic stress disorder, multiple chemical sensitivity, and irritable bowel syndrome. They also reported more evidence of cognition problems via the Cognitive Failure Questionnaire. The four multi-symptom conditions were all highly associated with one another and thus aggregated into a working case definition of Gulf War illness. Among the 3,831 (22% cases) Gulf War Seabee participants this case definition was then examined for potential associations with various demographic characteristics and 34 deployment exposures. Female, reserve, enlisted personnel of non-Seabee occupations, and belonging to two Seabee units were most likely to meet the case definition. Twelve self-reported Gulf War exposures were mildly associated with meeting the Gulf War illness definition with exposure to fumes from munitions having the highest odds (OR = 1.91; 95% CI 1.5-2.4). While these do not implicate a specific etiological exposure, they do shed new light on morbidity among Gulf War Seabees.

14. SUBJECT TERMS

Epidemiology, military personnel, Persian Gulf syndrome, military medicine, health survey, cross-sectional study, public health

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